Gestational Diabetes Flags Cardiovascular Risk

BY BRUCE JANCIN
Denver Bureau

DALLAS — Women with a history of gestational diabetes are at increased cardiovascular risk and deserve specific targeting for risk factor reduction, Kathleen King, Ph.D., said at the annual scientific sessions of the American Heart Association.

These women are particularly prone in middle age to an adverse lipid profile characterized by the combination of low HDL and elevated triglycerides, added Dr. King of the University of Rochester (N.Y.).

It's well established that women with a history of gestational diabetes mellitus (GDM) are at increased risk of developing type 2 diabetes. Since type 2 diabetes has been characterized by the National Cholesterol Education Program as a coronary heart disease risk equivalent, Dr. King and her coworkers hypothesized that women with a history of GDM would have a worse cardiovascular risk profile than those without such a history.

She reported on 17 women, mean age 44 years, with a history of GDM but without type 2 diabetes. They were matched with 17 controls by age, body mass index (BMI), and age of the index child, who on average was 14-15 years old. All participants underwent a 3-hour oral glucose tolerance test after 3 days on a 150-g carbohydrate/day diet followed by a 10-hour fast.

The mean triglyceride level was 140.9 mg/dL in women with a history of GDM, compared with 90.1 mg/dL in controls. Six women with prior GDM were hypertriglyceridemic as defined by a level in excess of 150 mg/dL, as was the case for only a single control subject.

Although mean HDL values didn't differ between the two groups, eight women with a history of GDM had an HDL below 50 mg/dL, compared with two controls. Five women with prior GDM, but none of the controls, had both low HDL and hypertriglyceridemia.

"This was true even though controls were matched for BMI. This indicates overweight and obesity in and of themselves may not be the only differentiating features between women with and without a history of GDM," she observed.

Unexpectedly, mean LDL in the group with prior GDM was lower than in controls: 100.7 mg/dL, compared with 110.1 mg/dL.

Three women with a history of GDM met NCEP criteria for the metabolic syndrome, as did one in the control group. But eight women with prior GDM met at least two of the five criteria for the metabolic syndrome, as did only three controls. ■

Lactation Lowers Maternal Type 2 Diabetes Risk Rate

BY MICHELE G. SULLIVAN
Mid-Atlantic Bureau

The longer a woman breast-feeds her offspring, the less likely she is to develop type 2 diabetes, Dr. Alison M. Stuebe, and her colleagues have reported.

Their analysis of more than 157,000 women concluded that every year of lactation results in a decreased risk of up to 15% for developing the disease. However, the association wasn't significant for women whose last child was born more than 15 years ago, said Dr. Stuebe of Brigham and Women's Hospital, Boston (JAMA 2005;294:2601-10)

The researchers examined lactation and disease occurrence in women enrolled in the two national Nurses' Health Studies. The studies provided more than 2 million person-years of follow-up from 1986 to 2002.

The Nurses' Health Study (NHS I) included 83,585 women; there were 5,145 incident cases of type 2 diabetes. The NHS II included 73,418 women; there were 1,132 incident cases of type 2 diabetes. In both studies, there was a slight, but significant, inverse association between length of lactation and disease risk.

However, when the researchers analyzed the groups by length of time since giving birth, the impact of breast-feeding became more apparent. Among 857 women who had given birth within the last 15 years, the risk reduction for each year of lactation was 15% in the NHS I and 14% in the NHS II. This association was stronger when women breast-fed for a total of at least 6 months. In the NHS I, the risk reduction was 26% for a cumulative lactation of up to 6 months, 36% for cumulative lactation of up to 1 year, and 53% for cumulative lactation of 23 months or more. The numbers were similar for women in the NHS II.

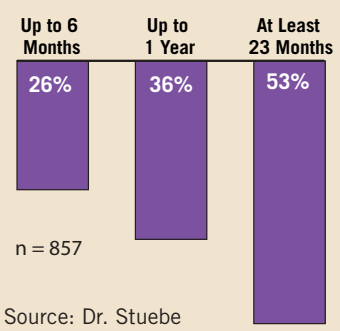
However, among women who reported their last birth more than 15 years ago, there was no association between the duration of lactation and diabetes. Likewise, there was no association between lactation and disease risk in women with gestational diabetes.

The researchers also found that pharmacological suppression of lactation was associated with an increased risk of developing type 2 diabetes. There was a 46% increased risk of disease in women who used medication to suppress lactation, compared with women who never breast-fed and did not use this type of medication.

The cause of this association is unknown. The investigators suggested that bromocriptine may disrupt mechanisms of appetite regulation or that a choice to suppress lactation may be associated with other behaviors that increase the risk of diabetes.

The decrease in development of diabetes among women who have breast-fed appears linked to lactation's effect on insulin resistance, the researchers said. Studies have shown that lactation is associated with improved glucose tolerance and fasting glucose levels. ■

Risk Reduction in Women Who Gave Birth Within the Last 15 Years
Cumulative Lactation



Source: Dr. Stuebe

Hopes for Fenofibrate in Diabetics Dashed, Primary End Point Unmet

BY BRUCE JANCIN
Denver Bureau

DALLAS — Expectations were high for a big positive result in the Fenofibrate Intervention and Event Lowering in Diabetes (FIELD) study, the largest-ever randomized prospective trial of cardiovascular intervention in type 2 diabetes.

Many on hand for the presentation of the FIELD results at the annual scientific sessions of the American Heart Association anticipated outcomes so favorable as to lift fenofibrate into the realm of first-line therapy in diabetic patients, joining the statins.

So when FIELD principal investigator Dr. Anthony Keech announced the study had failed to meet its primary end point, the fall was a hard one. Within hours the stock market knocked 7.3% off the value of Abbott Laboratories shares.

"What a shocker," Dr. Prakash C. Deedwania said in an interview. "The question after FIELD isn't any longer whether there should be increased fenofibrate use in patients with diabetes, it's whether there's any role for fenofibrate at all."

CATHERINE HACKETT

The study failed to meet its primary end point, but there were some positive secondary findings, Dr. Anthony Keech reported.

FIELD involved 9,795 patients with type 2 diabetes who were randomized in double-blind fashion to 200 mg fenofibrate daily or placebo. None were on statin therapy at baseline. After 5 years, the combined primary end point of nonfatal MI or death due to coronary heart disease (CHD) had occurred in 5.2% of patients on fenofibrate and 5.9% on placebo, a nonsignificant 11% reduction in relative risk. While nonfatal MIs were reduced by 24% in the fenofibrate group, CHD mortality increased by a nonsignificant 19%, said Dr. Keech, professor of medicine at the University of Sydney.

He termed the FIELD results "mixed." Bright spots included the positive secondary findings of a 21% reduction in coronary revascularization and an 11% reduction in total cardiovascular events, from 13.9% with placebo to 12.5%. For one additional cardiovascular event to be prevented, 70 patients would need to receive fenofibrate for 5 years.

The fenofibrate group also had significantly reduced albuminuria progression, fewer amputations, and less need for laser surgery for retinopathy. But Dr. Deedwania said what really matters in a very-high-risk population such as diabetic patients is whether lives are saved, and fenofibrate failed in this regard.

He shrugged off the improvement in diabetic end points. "That's not why you use the fibrates. We have better drugs for that: the PPAR [peroxisome proliferator-activated receptor] agonists," said Dr. Deedwania, professor of medicine and chief of the cardiology division for the University of California, San Francisco, Fresno Program.

A key factor in the failure to meet the primary study end point was that the landmark Heart Protection Study reported results midway through FIELD. In response, 17% in the placebo group were put on a statin by their physician, a rate more than twice as high as in the fenofibrate arm. That change clearly played a major role in the loss of fenofibrate's expected benefit, according to Dr. Ginsberg, professor of medicine and head of the division of preventive medicine and nutrition at Columbia University, New York.

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